PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference RE/PG4744	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB03/00336	International filing date *(day/month/year)* 23.01.2003	Priority date *(day/month/year)* 25.01.2002
International Patent Classification (IPC) or both national classification and IPC A61K9/16		
Applicant GLAXO GROUP LIMITED		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
04.08.2003	04.12.2003
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Giménez Miralles, J Telephone No. +49 89 2399-8655

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB03/00336

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-26 as originally filed

Claims, Numbers

1-24 as originally filed

Drawings, Sheets

1/16-16/16 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-24
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-24
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-24
	No:	Claims	

2. Citations and explanations

   see separate sheet

Re Item V

1) Reference is made to the following document:

D1: WO-A-95 19799

D2: WO-A-97 40839

D3: EP-A-1 138 337

2) The subject-matter of present claims 1-24 complies with the requirement of novelty as set forth in Article 33(2) PCT.

None of the prior art citations mentioned in the International Search Report anticipates a solid DNA dosage form for intradermal ballistic delivery of supercoiled plasmid DNA comprising: i) a supporting core (metal bead, e.g. gold or tungsten); coated with: ii) an amorphous solid reservoir (sugar in glassy form, e.g. trehalose, sucrose, etc.) containing the DNA agent and a stabilising agent (metal ion chelator such as inositol hexaphosphate, EDTA, TRIS, succinic acid, etc.; or a free radical scavenger such as ethanol, methionine or glutathione).

3) The subject-matter as defined in present claims 1-24 appears to involve an inventive step (Article 33(3) PCT).

The technical problem underlying the invention is to provide a delivery device suitable for needleless ballistic delivery of DNA vaccines into human skin (intradermal DNA vaccines), wherein the DNA agent is in a supercoiled form.

The closest prior art can be considered to be D1, which discloses metal (gold) particles coated with DNA plasmids by precipitation. D2 relates to the stabilization of supercoiled DNA in liquid solution by metal ion chelators or free radical scavengers. D3 relates to microneedles or microspheres comprising a glassy polyol matrix stabilizing the active agent. There is no suggestion in the state of the

art to combine the DNA-coated metal cores of D1 with the stabilizing glassy carrier described in D3. Moreover, the state of the art provides no hint to extrapolate the teaching of D2 to dry forms of supercoiled DNA coated onto gold or tungsten bead cores for ballistic intradermal delivery. Therefore, the combination of features as mentioned in item V-2 above appears to be non-obvious.